REMARKS

Claims 4 - 8, 15, 20 and 23 - 26 are rejected under 35 USC 112, first and second paragraphs, as the claimed invention is not described in such full, clear, concise and exact terms as to enable any person skilled in the art to make and use the same, and/or failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The Examiner gives the following reasons as support for this rejection:

> "1. "antiviral" is unclear. It reads on any and all viral infections, including AIDS viruses.
>
> 2. There is no adequate support that the instant compounds are useful for the urged utility, such as treating retroviruses, AIDS or AID-related diseases. Applicant has provided in vitro test data of two compounds within the instant scope against four viruses and their cytopathogenic effect on HIV. It is well-known that those skilled in the art would not associate successful in vitro results with successful in vivo efficacy. One skilled in the art would not accept the in vitro testing set forth in the present specification as a proper basis to conclude that instantly claimed compounds are useful in in vivo treatment of humans afflicted with retroviral diseases.
>
> Furthermore, the test data (Table I) is not clearly understood. Does applicant intend a range of dosage? It is noted that higher dosage is twice of lower dosage. Since ID_{50} is the minimum drug conc. that inhibits CPE by 50%, the data is of no statistic significance. As for VZV and/or HCMC, the ID_{50} is unclear. What is >96 or >38? 400? 600? 1000? The data further support that antiviral activity is unpredictable. The specification does not commensurate with the scope of the claim. Ex parte Balzarini, 21 USPQ 2d 1892."

Claims 4 - 8, 15, 20, and 23 - 26 are rejected under 35 USC 101. The Examiner states that:

> "although the in vitro testing appears to be useful as a screening tool in order to determine which compounds are candidates for further test to see if they possess in vivo utility. The in vitro tests are not predictive of in vivo efficacy. Furthermore, compounds where R_1 as
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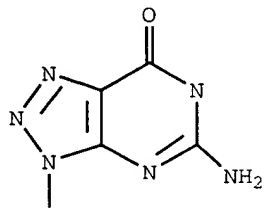
> 
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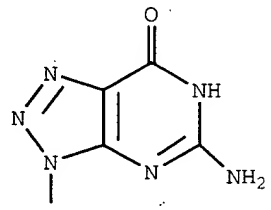
> are not a purine derivative and is not commonly recognized as the base of the analog of AZT type compound.
>
> As discussed under 112 rejection, antiviral activities are unpredictable. Only two compounds have been in vitro tested. There is no reasonable assurance that claimed compounds have in vivo efficacy in the treatment of retroviral diseases broadly or specifically AIDS. Ex parte Balzarini, supra."

Claims 25 and 26 have been amended in accordance with the specification at page 5, lines 30 to 32 and the data given at page 106 of the specification. Applicants submit that in view of these amendments all of claims 4 - 8, 15, 20 and 23 - 26 are in full compliance with the requirements of 35 USC 112, first and second paragraphs as well as 35 USC 101.

With respect to the specific points raised by the Examiner, the claims no longer read on all viral infections including AIDS and other retroviruses. Thus, the decision in Ex parte Balzarini is not applicable to the instant claims. The use of a range for the ID_{50} at pages 106 and 107 simply means that at the dilution concentrations employed, a 50% reduction did not

occur. Thus, the dilution below and the dilution above the 50% inhibition levels are listed meaning that the 50% inhibition concentration is somewhere in between these two concentrations. The greater than number means that 50% inhibition did not occur at concentrations up to that level which was the last concentration tested.

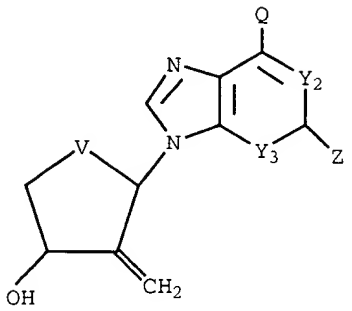
With respect to the rejection of Claims 4 - 8, 15, 20, and 23 - 26 under 35 USC 101, applicants submit that such rejection is improper since the claims are directed to novel compounds and their use as antiviral agents against specific DNA type viral infections. These claims are not directed to the treatment of retroviral diseases as in the Balzarini case. Also, there is no disclosure that compounds wherein R_1 is



are useful in treating retroviral disease.

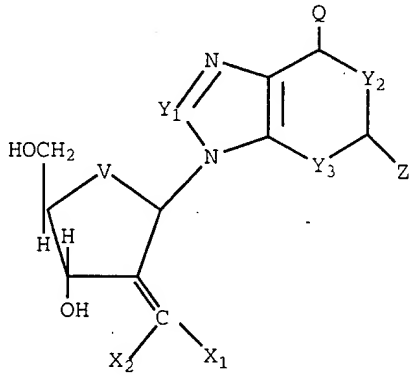
Claims 4 - 8, 15, 20 and 23 - 26 are rejected under 35 USC 102(a) or 102(e) as anticipated by or, in the alternative, under 35 USC 103 as obvious over EP 365,849. The Examiner states that:

"EP discloses compounds of

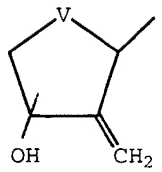


wherein V can be methylene; Y_2 and Y_3 can independently be nitrogen or CH; Q is NH_2, NHOH, $NHCH_3$ or hydrogen; Z is hydrogen, halo or NH_2, useful in inhibiting AdoMet-dependent transmethylation and in the treatment of patients afflicted with neoplastic or viral diseases. The instantly claimed compounds are taught therein and are obvious thereover in view of the structural activity."

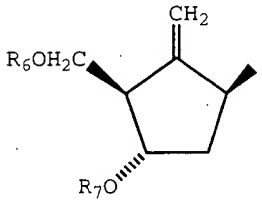
Applicants note that MaCarthy et al. (EP 365,849), as discussed previously, in fact disclose compounds of the formula



wherein at least one of X_1 and X_2 is halogen. Thus, there is <u>no</u> disclosure in 365,849 of



Also, there is no disclosure in 365,849 of the cyclopentyl ring system



recited in the instant claims.

Thus, the disclosure in 365,849 clearly does not anticipate the instant claims under 35 USC 102(a) or (e). With respect to the obviousness rejection, the Examiner has failed to suggest why one of ordinary skill in the art would be motivated to replace or modify the cyclopentyl ring of McCarthy et al. so as to arrive at the cyclopentyl ring of the instant claims and how such modification could be achieved.

Further, applicants direct the Examiner's attention to the accompanying Rule 131 Declaration showing a completion of the claimed invention in the United States before the May 2, 1990 publication of EP 365,849. Thre subject matter of instant claims 4 - 8, 15, 20 and 23 - 26 are fully supported by the specification and claims in abandoned parent application Serial No. 599,568 filed October 18, 1990. The Declaration clearly establishes that the compound of Claim 15 which is within the genus of Claims 23 - 26 and 4 - 7 was made, tested, and found to

possess antiviral activity in the United States prior to May 2, 1990.

For these reasons, applicants submit that this application is now in condition for allowance.

Respectfully submitted,

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SBD:pap